

REMARKS

Upon entry of the present amendment, claims 39-66 will be pending in the present application.

Claims 39, 44, 50, 51, and 59 are amended to clarify the subject matter Applicants regard as their invention. Support for the amendment to claims 39, 50, 51, and 59 in which the term “porous” is added is found in the specification as filed at page 34, line 33 through page 35, line 6, and at page 62, lines 15-19. Claim 59 is further amended to replace the term “condition” in the body of the claim with its antecedent, “disorder,” as recited in the preamble. Similarly, claim 44 has been amended to recite that the cessation of blood flow is that “out of the breached vessel,” to be consistent with claim 43, upon which it depends.

All the amendments to the claims are fully supported by the specification as filed. No new matter has been added.

The Rejection Under 35 U.S.C. § 112, Second Paragraph Should be Withdrawn

Claims 39-66 are rejected under 35 U.S.C. § 112, second paragraph as allegedly indefinite. In particular, in section 7 of the Office Action, it is alleged that the phrase “non-barrier forming,” is unclear.

The legal standard for clarity under 35 U.S.C. § 112, second paragraph, has been expressed as follows:

Determining whether a claim is definite requires an analysis of whether one skilled in the art would understand the bounds of the claim when read in the light of the specification. If the claims read in light of the specification reasonably apprise those skilled in the art of the scope of the invention, § 112 demands no more. (*Solomon v Kimberly-Clark* 216 F.3d 1374, 1378 (Fed. Cir. 2000))

In light of the instant specification, Applicants submit that those of skill in the art would appreciate that “non-barrier forming” materials, as recited in the instant claims, are porous materials that do not “provide a mechanical matrix that adheres to the site of application and seals the boundaries” of a wound (page 12, lines 11-13 of the specification as filed). Moreover, the skilled worker would understand that, in this context, such porous, non-barrier forming materials could be formulated, *e.g.*, as porous gels, sponges, films, or

membranes, or could be formulated as foams, sprays, emulsions, suspensions, or solutions, that comprise the recited poly- β -1 \rightarrow 4 N-acetylglucosamine polymers.

Therefore, Applicants respectfully submit that claims 39, 50, 51, and 59, when read in the light of the specification as filed, clearly apprise those skilled in the art of the scope of the claimed invention. Since § 112 requires no more than this, Applicants respectfully submit that the phrase “non-barrier-forming,” as recited in claims 39, 50, 51, and 59, as amended, is not unclear. Accordingly, Applicants respectfully request that the rejection of claims 39-66 under 35 U.S.C. § 112, second paragraph be withdrawn.

The Rejection Under 35 U.S.C. § 103(a) Should be Withdrawn

Claims 39-66 are rejected under 35 U.S.C. § 103(a), allegedly as obvious over U.S. Patent No. 5,635,493 to Vournakis *et al.* (“Vournakis”), in view of Barton *et al.* (1999) *Curr. Opin. Nephrol. Hypertens.* 8: 549-556 (“Barton”) and Pearson *et al.* (2000) *Lupus* 9: 183-188 (“Pearson”), for the reasons provided below. Applicants respectfully traverse this rejection.

In an attempt to support this rejection, the Examiner alleges, in section 11, at page 7 of the Office Action, that

It would have been obvious to one of ordinary skill in the art at the time of the invention to combine the teachings of the prior art [Vournakis, Barton, and Pearson] to arrive at the instantly claimed invention. It would have been obvious to one of ordinary skill in the art at the time of the invention that the method described by Vournakis would also induce the release of endothelin-1 and vasoconstriction since Vournakis teaches that the GlcNac materials may be used to promote hemostasis and wound healing, and the prior art [Barton and Pearson] teaches that normal endothelial cell function is critical for all aspects of vascular homeostasis.

At page 7 of the Office Action, the Examiner further contends that

It would have also been obvious to the skilled artisan that the more GlcNac composition applied to a wound or breached blood vessel, the more bleeding would be reduced.

At page 7, the Examiner asserts that: “One would have been motivated to do so [combine the teachings of Vournakis, Barton, and Pearson] in order to treat skin wounds and reduce wrinkles.”

Legal Standards for a Determination of Obviousness Under 35 U.S.C. § 103(a)

The legal standard of *prima facie* obviousness requires that three criteria be met: (1) the prior art, either alone or combination, must teach or suggest each and every limitation; (2) a suggestion or motivation in the cited references or in the art to modify or combine the cited references; and (3) the cited references must provide a reasonable expectation of successfully achieving the claimed invention. *In re Vaeck*, 20 U.S.P.Q.2d 1438, 1442 (Fed. Cir. 1991); *In re Wilson*, 165 U.S.P.Q. 494, 496 (CCPA 1970). Applicants respectfully submit that *prima facie* obviousness has not been established since these criteria are not met.

Accordingly, the mere listing of elements or attributes of elements that may be discovered or alleged in the prior art, without more, simply amounts to “hindsight reconstruction...using the patent in suit as a guide through the maze of prior art references, combining the right references in the right way so as to achieve the result of the claims in suit.” (*Grain Processing v. American Maize-Products* 5 USPQ2d 1788, 1792 (Fed. Cir. 1992) (citation and internal quotation omitted).

The Court of Appeals for the Federal Circuit has “made it clear that the best defense against the subtle but powerful attraction of a hindsight-based obviousness analysis is rigorous application of the requirement for a showing of the teaching or motivation to combine the prior art references.” (*In re Dembiczak* 50 USPQ2D 1614, 1617 (Fed. Cir. 1999)). The Court of Appeals for the Federal Circuit has also provided that

Where claimed subject matter has been rejected as obvious in view of a combination of prior art references, a proper analysis under § 103 requires, *inter alia*, consideration of two factors: (1) whether the prior art would have suggested to those of ordinary skill in the art that they should make the claimed composition or device, or carry out the claimed process; and (2) whether the prior art would also have revealed that in so making or carrying out, those of ordinary skill would have a reasonable expectation of success. Both the suggestion and the reasonable expectation of success must be founded in the prior art, not in the applicant’s disclosure. (*In re Vaeck* 20 USPQ2d 1438, 1442) (Fed. Cir. 1991) (internal citations omitted)

The claims, as currently pending, recite use of porous materials comprising the recited poly-β-1→4 N-acetylglucosamine polymers to induce a transient, localized modulation of vascular structure and/or function or to ameliorate a vascular disorder. Vournakis teaches that barrier-forming materials comprising p-GlcNac can be used to seal the edges of a wound in order to achieve hemostasis, and that such materials create a physical barrier to blood flow

and that supports and protects clot formation. (Vournakis, col. 35, lines 38-52; Col. 61, line 8 to Col. 62, line 42). Porous, non-barrier-forming materials, by definition however, would not *inter alia* seal the boundaries of a wound. Thus, Vournakis does not teach or suggest the use of porous non-barrier-forming materials comprising p-GlcNac to induce transient, localized physiological responses and/or a transient, localized, modulation of vascular structure and/or function. Applicants assert, therefore, that the teaching in Vournakis would not suggest or provide a reasonable expectation of success for methods that utilize porous materials (that is, materials that allow flow of gases or liquids) to achieve the result recited in the pending claims.

Pearson describes some seventeen proteins and two small molecules (NO and prostaglandin PGI₂) that are involved in clot formation, clot removal and the regulation thereof, and provides a general summary of a number of physiological functions attributed to endothelial cells, including their involvement in the control of coagulation and fibrinolysis and the maintenance of vascular homeostasis (page 185, second column, through page 186, second column, second paragraph).

Barton describes the role played by endothelin-1 in vasoconstriction and the possible role that increased levels endothelin-1 may play in hypertension and renal disease (*see* the abstract at page 549).

Neither of the secondary references (Pearson and Barton), even mention any material comprising pGlcNac. Further, Pearson provides no teaching regarding administration, much less topical administration, of compounds that induce a transient, localized modulation of vascular structure and/or function. Likewise, Barton provides no indication that compounds can be topically administered or that administered compounds would exhibit local activity. Thus, neither Pearson nor Barton, either alone or in combination with each other and Vournakis, teach or suggest use of the presently-recited porous non-barrier-forming material comprising pGlcNac (a) to induce a transient, localized modulation of vascular structure and/or function or (b) to ameliorate a vascular disorder.

Moreover, the combination of references cited by the Examiner fail to render obvious the dependent claims that recite methods resulting in stimulation of endothelin-1 release. The Examiner acknowledges that Vournakis does not teach endothelin release or vasoconstriction. (p. 6 of the Office Action) The secondary references (Pearson and Barton) merely observe that endothelial cells play a role in vascular homeostasis. This simply does not provide a

logical basis for, or an inferential route to, a conclusion that topical administration of the presently-recited materials can stimulate release of endothelin-1 and induce vasoconstriction. This information is only available in the specification as filed, and use of this information in an attempt to support a rejection based on obviousness would constitute an impermissible use of hindsight.

Likewise, the fact that transient physiological effects induced according the presently-claimed methods directed toward modulation of vascular structure and/or function have been shown be substantially proportional to the amount of p-GlcNac-containing material applied is first observed in the instant application. Accordingly, Applicants respectfully submit that the basis for the Examiner's contention that it would have been obvious that "the more GlcNac composition applied to a wound or breached blood vessel, the more bleeding would be reduced," is also based solely upon information that is only available in the instant specification, and, as such, constitutes an impermissible use of hindsight in attempting to create an obviousness rejection.

Applicants further submit that the Examiner has provided no motivation for combining the cited art in an attempt to arrive at the presently-claimed invention. Applicants respectfully submit that a generic desire to treat a broadly-defined disease or condition and the specific motivation to combine particular pieces of art to arrive at a specifically-claimed invention are not one and the same. Thus, although the Examiner has alleged the existence of a generic goal of treating "skin wounds and reducing wrinkles," the Examiner has not pointed to any motivation to combine the cited art in order to arrive at the presently-claimed methods that are directed toward the modulation of vascular structure and/or function and the amelioration of a vascular disorder.

Assuming, *arguendo*, that the rejection under § 103(a) was proper, and that there was motivation to combine the cited art, that combination would not have provided a reasonable expectation of success to one of ordinary skill in the art.

As noted above, the cited art, even collectively, does not teach or suggest methods that use porous, non-barrier forming materials comprising p-GlcNac to induce at least a transient, localized physiological responses and/or a transient, localized, modulation of vascular structure and/or function. As also noted, above, the teaching provided by Vournakis that pGlcNac be used to achieve hemostasis by sealing the boundaries of a wound, and by supporting and promoting blood clot formation at the site of the wound. Such a generation of

a physical barrier to blood flow, however, would fail to provide one of ordinary skill in the art with a reasonable expectation of success for a method that, in contrast, achieves at least a transient localized modulation of vascular structure and/or function by using a porous pGlcNAc material.

Consequently, in view of all of the above, Applicants respectfully submit that independent claim 39 and 59, and therefore ¹ claims 40-66 dependent thereon, are not obvious over the combination of Vournakis, Barton, and Pearson. Accordingly, Applicants respectfully request that the rejection of claims 39-66 as obvious under 35 U.S.C. § 103(a) over Vournakis, Barton, and Pearson, be withdrawn.

CONCLUSION

Applicants believe that each ground of rejection of the pending claims has been successfully overcome or obviated. Accordingly, Applicants respectfully request that the rejection of claims 39-66 under 35 U.S.C. §§ 103 and 112 be withdrawn.

Applicants submit that the entire application is now in condition for allowance, early notice of which would be appreciated. Should the Examiner not agree with Applicants' position, then a personal or telephonic interview is respectfully requested to discuss any remaining issues and expedite the eventual allowance of the application.

The Commissioner is hereby authorized to charge any required fee(s) to Jones Day Deposit Account No. 50-3013.

Respectfully submitted,

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¹ "Dependent claims are nonobvious under section 103 if the independent claims from which they depend are nonobvious." *In re Fine* 5 USPQ2d 1596, 1600 (Fed. Cir. 1988)